

Children with epilepsy: are they the same on both sides of the Atlantic, and do the same treatments work?

It is often said, but rarely written, that diagnostic and treatment attitudes differ between European and US epileptologists. A variety of reasons are put forward when one tries to defend such a position: the great contribution of European epileptology to the description of the electro-clinical semiology of seizures and the definition of epilepsy syndromes; the great contribution of US colleagues to fundamental research into the underlying mechanisms of action of AEDs; the more extensive facilities in the US, allowing combination of clinical and fundamental research, as compared to facilities in Europe; differences in prescription rules; the role and history of the FDA as compared to the more recently created (1995) European Agency for the Evaluation of Medicinal Products (EMA); differences between the various European countries in the licensing of various AEDs; the fact that most of the early phases of drug development are performed in the USA, etc.

In 2005, J. Wheless, D. Clarke and D. Carpenter published results of the first expert survey performed in the United States (Wheless *et al.* 2005), of the treatment of pediatric epilepsy. It was the US survey that gave us the idea to perform a similar survey in Europe, involving child neurologists that regularly treat children with epilepsy. The limits, possible biases, and the benefits of such surveys are beyond the scope of this editorial but are fully discussed in the article published in this issue of *Epileptic Disorders*. However, an objective of the European survey was to have a similar structure, thus allowing direct comparison of practices between US and European experts in the field. Several interesting observations can be made in the two surveys when comparing suggestions for initial monotherapy.

– For *symptomatic myoclonic and generalized tonic-clonic seizures*, both groups consider a wide-spectrum AED, valproate, being the treatment of choice. However, the US experts also consider lamotrigine and topiramate as appropriate (first-line) options, while in Europe these two AEDs, in addition to levetiracetam, are considered as high ranked, second-line options, with lamotrigine being pre-

ferred to the other two. Zonisamide, not available in Europe at the time of the survey, is also considered “usually appropriate” in the US.

– Even more interesting is the comparison of choices for the treatment of *focal epilepsies* (complex partial seizures), with carbamazepine and oxcarbazepine occupying the first place for both expert groups. These two AEDs are closely followed by valproate as a first-line choice for the Europeans, a drug considered only “sometimes appropriate” by US colleagues, who clearly prefer lamotrigine, levetiracetam and topiramate before valproate. Levetiracetam was not licensed as a first choice treatment in Europe at the time of the survey.

– For *neonatal seizures*, both groups use IV phenobarbital, with IV lorazepam (not available in many European countries) or IV fosphenytoin being the alternative first choices in the US. Lack of IV formulations for the majority of AEDs and lack of controlled studies in neonates probably explain the choice of phenobarbital.

– For *infantile spasms* secondary to tuberous sclerosis, both groups have a clear preference for vigabatrin (closely followed by ACTH in the US, where vigabatrin is not commercialized). However, for symptomatic infantile spasms other than those seen in tuberous sclerosis patients, vigabatrin still occupies the first position in Europe (followed by ACTH and prednisone), while the US group rank vigabatrin only fourth, after ACTH, topiramate and zonisamide. Valproate occupies a similar position in both groups.

– For the treatment of *Lennox-Gastaut syndrome*, both groups have a clear preference for valproate as a first choice, the alternatives, by order of preference being lamotrigine and topiramate for the Europeans versus topiramate and lamotrigine for the US experts. Both expert groups considered zonisamide, levetiracetam, the ketogenic diet, felbamate and the benzodiazepines as sometimes appropriate (high second line) for such patients.

– For the management of acute, prolonged, *febrile seizures* or clusters of febrile seizures, both expert groups use rectal diazepam as a first choice. However, when preven-

tive treatment is decided, European experts have a clear preference for valproate while US experts will first try phenobarbital and eventually consider valproate.

– A very clear difference in treatment approaches was observed for *Rolandic epilepsy*, when therapy is considered necessary. Valproate was a clear first choice for the European experts, with carbamazepine, oxcarbazepine and sulthiame considered as “sometimes appropriate”. For the US experts, valproate was ranked fifth, after oxcarbazepine, carbamazepine, gabapentin, lamotrigine and levetiracetam.

– For epilepsies with *typical absences* as the predominant type of seizure, both approaches are quite similar. In cases of childhood absence epilepsy, the US experts have a preference for ethosuximide before valproate, which is the European preference, with lamotrigine occupying the third position in both. When it comes to the treatment of juvenile absence epilepsy, both groups would choose valproate first, with lamotrigine being a close alternative for the US experts.

– A *male patient with juvenile myoclonic epilepsy* would be started on valproate as first choice treatment in both continents, followed by lamotrigine for both groups. Levetiracetam would be a “sometimes appropriate” third choice for the Europeans while topiramate would be tried before levetiracetam in the US (to be noted that the studies on levetiracetam for the control of myoclonic seizures were not available at the time of the US survey). The strategy would be similar in both groups in the case of a *female patient*, with lamotrigine occupying the first posi-

tion. This common position probably reflects good knowledge of the pregnancy registries results.

– Another clear difference was found in the treatment of *newly diagnosed epilepsy* at the emergency department. In Europe the great majority of experts rated valproate as extremely appropriate as first treatment. What is perhaps surprising, is the selection by the US experts of carbamazepine as the first-line option for a child whose seizure type or epilepsy syndrome is often not clear.

– No major difference was noted in attitudes towards treatment of *convulsive status or non-convulsive status epilepticus*, with the exception that IV lorazepam, not easily available in most European countries, is used before IV diazepam in the US.

Overall, we can conclude that US and European experts have a similar approach towards the majority of epilepsy syndromes. This probably reflects the successful merging of the two scientific communities in recent years, the regular participation in International, European and American epilepsy meetings, and easier access to the literature. However, valproate is the clear preference of European child neurologists, while US experts seem to be less reluctant to use newer antiepileptic drugs. □

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Reference

Wheless JW, Clarke DF, Carpenter D. Treatment of pediatric epilepsy: expert opinion, 2005. *J Child Neurol* 2005; 20: 51-6.